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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/806,876	04/05/2001	Marion Ress-Loschke	49462	7706

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WASHINGTON, DC 20036

EXAMINER

FRONDA, CHRISTIAN L

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 06/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/806,876

Applicant(s)

Ress-Loschke et al.

Examiner

Christian L. Fronda

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (e). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on _____
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-15 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on Apr 5, 2001 is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 1 and 3 6) ☐ Other:

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DETAILED ACTION

1. Claims 1-15 are under consideration in this Office Action.

Claim Rejections - 35 U.S.C. § 101

2. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. Claims 2, 3, 6, and 7 are rejected under 35 USC 101 because the claimed invention is directed to non-statutory subject matter.

Claims 2, 3, 6, and 7 as written, do not sufficiently distinguish over nucleic acids, proteins, cells or antibodies as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). *See* MPEP 2105.

Amending claims 2 and 3 to recite the phrase "an isolated polypeptide" may overcome this rejection. Amending claims 6 and 7 to recite the phrase "a transformed bacterial host cell" may overcome this rejection.

Claim Rejections - 35 U.S.C. § 112, 1st Paragraph

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 2, and 4-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid encoding a nitrilase comprising the amino acid sequence of SEQ ID NO: 2 or an isolated nucleic acid of SEQ ID NO: 1 encoding a nitrilase; does not reasonably provide enablement for any other embodiment. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly

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connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *re Wands* [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The *Wands* factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claims encompass any isolated nucleic acid encoding any nitrilase having any amino acid that is at least 95% homologous to SEQ ID NO:2. The specification provides guidance and examples for making an isolated nucleic acid encoding a nitrilase comprising the amino acid sequence of SEQ ID NO: 2 or an isolated nucleic acid of SEQ ID NO: 1 encoding a nitrilase.

However, the specification does not teach the specific catalytic amino acids and the structural motifs which are essential for enzyme structure and activity/function. The state of the art as exemplified by Attwood et al. (Comput. Chem. 2001, Vol. 25(4), pp. 329-39) is such that "...we do not fully understand the rules of protein folding, so we cannot predict protein structure; and we cannot invariably diagnose protein function, given knowledge only of its sequence or structure in isolation" (see Abstract and entire publication). Furthermore, Ponting (Brief. Bioinform. March 2001, Vol. 2(1), pp. 19-29) states that "...predicting function by homology is a qualitative, rather than quantitative, process and requires particular care to be taken...due attention should be paid to all available clues to function, including orthologue identification, conservation of particular residue types, and the co-occurrence of domains in proteins" (See Abstract and entire publication).

The standard for meeting the enablement requirement is whether one of skill in the art can make the invention without undue experimentation. The amount of experimentation to make the claimed polynucleotides is enormous and entails selecting specific nucleotides to change (nucleotide deletion, insertion, substitution, inversion, or combinations thereof) in a polynucleotide encoding SEQ ID NO: 2 and determining by enzymatic assays whether the polynucleotide encodes a protein that has nitrilase activity. The specification does not provide guidance with respect to the specific catalytic amino acids and the structural motifs essential for enzyme structure and activity/function which must be preserved. Thus, the amount of experimentation to make the claimed invention is well outside the realm of routine experimentation and predictability in the art of success in determining whether the resulting polynucleotide encodes a protein that has nitrilase activity is extremely low since no information is provided by the specification regarding the specific catalytic amino acids and the structural motifs essential for enzyme structure and activity/function which must be preserved.

The Examiner finds that one skilled in the art would require additional guidance, such as information regarding the specific catalytic amino acids and the structural motifs essential for

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enzyme structure and activity/function which must be preserved. Without such a guidance, the experimentation left to those skilled in the art is undue.

Claim Rejections - 35 U.S.C. § 112, 2nd Paragraph

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
7. Claim 1-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite because the meaning of the phrase "as a result of the degeneracy of the genetic code" is not known. Furthermore, the phrase "negligible reduction in the enzymatic action of the polypeptide" renders the claim vague and indefinite because the metes and bounds of "negligible reduction in enzymatic action" are not known. Claims 2-15 which depend from claim 1 are also rejected because they do not correct the defect of claim 1.

Claims 2 and 3 are vague and indefinite because it is not known if the invention claimed is directed toward an isolated polypeptide or protein.

Claim 8 is vague and indefinite because it is not known how the claimed process can prepare chiral carboxylic acids in the presence of an "amino acid sequence". Claims 9-15 which depend from claim 8 are also rejected because they do not correct the defect of claim 8. Amending the claim to recite a process that uses isolated polypeptide or protein having the amino acid sequence of SEQ ID NO: 2 or encoded by the polynucleotide having the nucleotide sequence of SEQ ID NO: 1 may overcome the rejection. Furthermore, the phrase "growing, dormant or disrupted microorganism" is vague and indefinite because the meaning of the phrase is not known.

Claims 11 and 13 are vague and indefinite because the meaning of the phrase "[sic]" is not known and not recited in the claim.

Claim Rejections - 35 U.S.C. § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1, 4, 5, 6, and 7 is rejected under 35 U.S.C. 102(b) as being anticipated by Kobayashi et al. (Accession D13419; Nitrilase in biosynthesis of the plant hormone indole-3-acetic acid from indole-3-acetonitrile: cloning of the *Alcaligenes* gene and site-directed mutagenesis of cysteine residues. Proc. Natl. Acad. Sci. U.S.A. 90 (1), 247-251 (1993)).

Kobayashi et al. teach a polynucleotide sequence which encodes a nitrilase having at least 96.09% identity to SEQ ID NO: 2, vector containing said polynucleotide sequence, and bacterial host cell comprising said vector (see Accession D13419; and Nitrilase in biosynthesis of the plant hormone indole-3-acetic acid from indole-3-acetonitrile: cloning of the *Alcaligenes* gene and site-directed mutagenesis of cysteine residues. Proc. Natl. Acad. Sci. U.S.A. 90 (1), 247-251 (1993)). Thus, the reference teachings anticipate the claimed invention.

10. Claim 2 is rejected under 35 U.S.C. 102(b) as being anticipated by Kobayashi et al. (Accession A47181; Nitrilase in biosynthesis of the plant hormone indole-3-acetic acid from indole-3-acetonitrile: cloning of the *Alcaligenes* gene and site-directed mutagenesis of cysteine residues. Proc. Natl. Acad. Sci. U.S.A. 90 (1), 247-251 (1993)).

Kobayashi et al. teach a nitrilase having at least 96.09% identity to SEQ ID NO: 2 encoded by the nucleotide sequence Accession D13419, vector containing said polynucleotide sequence, and bacterial host cell comprising said vector (see Accession D13419; and Nitrilase in biosynthesis of the of the plant hormone indole-3-acetic acid from indole-3-acetonitrile: cloning of the *Alcaligenes* gene and site-directed mutagenesis of cysteine residues. Proc. Natl. Acad. Sci. U.S.A. 90 (1), 247-251 (1993)). Thus, the reference teachings anticipate the claimed invention.

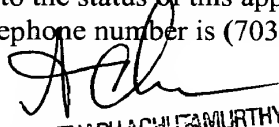
Conclusion

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L. Fronda whose telephone number is (703)305-1252. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703)308-3804. The fax phone number for this Group is (703)308-0294. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703)308-0196.

CLF

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